Application Serial No.: 09/527,352

IN THE CLAIMS:

Please amend the claims as follows:

1-104. (Canceled)

105. (Currently Amended) A method of screening a xenobiotic for susceptibility to biliary excretion, the method comprising the steps of:

(a)   establishing first and second cultures of hepatocytes, each culture comprising at least one bile canaliculus, the first culture having intact bile canaliculi and the second culture having disrupted bile canaliculi;

(b)   exposing a xenobiotic to the first culture and to the second culture for a time (T) sufficient to allow uptake of the xenobiotic;

(c)   washing and then lysing the first and second cultures;

(d)   measuring an amount of xenobiotic present in a lysate obtained from each culture in step (c); ~~and~~

(e)   calculating a <u>mass in the bile canaliculi as the difference in the amount of xenobiotic present in the lysates from</u> ~~biliary clearance value derived from~~ the first culture having intact bile canaliculi and the second culture having disrupted bile canaliculi ~~using the amount of xenobiotic in each culture lysate measured in step (d)~~; <u>and</u>

<u>(f)   calculating a biliary clearance value as the ratio of the mass in the bile canaliculi in step (e) and the area under the curve (AUC) in culture medium, wherein the AUC represents the integral of xenobiotic concentration in the medium from time 0 to time T,</u> to thereby screen the xenobiotic for susceptibility to biliary excretion.

106.   (Previously Presented)   The method of claim 105, wherein the hepatocytes are isolated from a source selected from the group consisting of rat, human, monkey, ape, cat, dog, pig, hog, cattle, oxen, sheep, horses, turkeys, chickens, ducks and geese.

2

107. (Previously Presented) The method of claim 105, wherein the first and second cultures of hepatocytes each further comprise a long-term culture of hepatocytes.

108. (Previously Presented) The method of claim 105, wherein the first and second cultures of hepatocytes further comprise a canalicular network.

109. (Previously Presented) The method of claim 105, wherein the first and second cultures of hepatocytes are further characterized as having a configuration selected from the group consisting of clusters of hepatocytes, aggregates of hepatocytes, at least one layer of hepatocytes, and combinations thereof.

110. (Previously Presented) The method of claim 105, wherein the hepatocytes are embedded in a matrix.

111. (Previously Presented) The method of claim 105, wherein the first and second cultures of hepatocytes further comprise a sandwich culture of hepatocytes, the sandwich culture comprising at least one layer of hepatocytes and at least one bile canaliculus with the at least one layer of hepatocytes.

112. (Previously Presented) The method of claim 111, wherein the at least one layer of hepatocytes is sandwiched between two layers of matrix.

113. (Previously Presented) The method of claim 111, wherein the first and second cultures of hepatocytes each further comprise a long-term culture of hepatocytes.

114. (Previously Presented) The method of claim 110, wherein the matrix is selected from the group consisting of a biological matrix medium, a synthetic matrix medium, and combinations thereof.

3

Application Serial No.: 09/527,352

115. (Previously Presented) The method of claim 114, wherein the biological matrix medium is selected from the group consisting of collagens, laminins, basement membrane-derived complexes, derivatives thereof and combinations thereof.

116. (Previously Presented) The method of claim 105, wherein steps (a) through (d) are carried out in at least one well of a multi-well plate.

117. (Previously Presented) The method of claim 105, further comprising screening a plurality of xenobiotics simultaneously for susceptibility to biliary excretion.

118. (Previously Presented) The method of claim 105, further comprising the step of differentiating between a xenobiotic that is not excreted in bile, a xenobiotic that is highly excreted in bile, and a xenobiotic that is readily and extensively excreted in bile.

119-200. (Canceled)

4